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Aortic valve regurgitation frequency following catheter ablation of premature ventricular complexes originating from coronary cusps

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ABSTRACT

Aims: There are conflicting results about the effect of radiofrequency catheter ablation (RFA) of aortic cusp premature ventricular complexes (PVCs) on aortic valve regurgitation (AR). We aimed to investigate the effect of aortic valve function and integrity of RFA of coronary cusp PVCs.

Methods: This cross-sectional study included 54 patients who underwent RFA of the aortic cusp region within the specified indications. Basal echocardiography was performed at baseline and 3 months after radiofrequency catheter ablation of aortic cusp PVCs. An increase of more than 1 degree in AR was considered significant.

Results: The mean age of the patients was 44.6±12.0 years and the male gender ratio was 42.6%. On 24-hour rhythm holter monitoring, the mean VES burden was 21.5%, of which 12.9% were right coronary cusp (RCC), 59.3% left coronary cusp (LCC), and 27.8% RCC-LCC junction. Total procedure time was 136.9±33.2 minutes and RFA time was 14.9±11.4 minutes. When pre- and post-ablation parameters were compared, left ventricular ejection fraction was found to be higher after the procedure than before the procedure ($p<0.001$). There was no statistically significant increase in the degree of AR before and after the procedure ($p>0.05$).

Conclusion: There was no increase in the degree of AR as a procedure-related complication and no significant AR was determined in patients who underwent RFA for PVCs in the aortic cusp region. Therefore, it can be concluded that VES ablations in the aortic cusp region are safe for the development of AR.

Keywords: Premature ventricular complexes, radiofrequency ablation, aortic cusp, aortic regurgitation

INTRODUCTION

Premature ventricular complexes (PVCs) are extremely common in general population. PVCs has a prevalence of 1-4% of the general population on standard electrocardiogram 12 leads, even it may reach 40-75% of subjects undergoing Holter monitoring.[1] PVCs may cause symptoms as palpitation, discomfort in chest or neck, strong heartbeat sensation, feeling of heart stopping, presyncope, dyspnea, fatigue. But the most feared complication of PVCs is PVC- induced cardiomyopathy (PVC-CMP). The treatment goal of the PVC s is not only decreasing the symptom burden of the patient but also preventing the PVC-CMP development or if exists reversing the CMP. Coronary cusp originated PVCs constitutes an important and common site for PVCs. Although different percentages are reported at different studies; 37% of PVCs originates from right ventricular outflow tract, 25% of from coronary cusp, 3% of from aortomitral continuity, 10% of from left ventricular (LV) summit/epicardial, 8% of from parahisian and 3% of from multiple foci.[2]

Treatment strategies for PVCs are radiofrequency catheter ablation (RFA) and medical treatment. Rarely seen complications of RFA are vascular access site hematoma, pericardial effusion, injury of coronary artery or veins, atrioventricular complete block. There are not many studies studying effect of RFA on aortic valve functions and integrity. Minich et al.[3] demonstrated a 30% increase in the incidence of aortic valve regurgitation (AR) after RFA of left-sided accessory connection. Edward et al.[4] reported that cusp ablation did not cause aortic valve dysfunction. Kis Z et al.[5] reported a case that aortic valve leaflet rupture following RFA of LV originated PVCs at a 72 years old man. Although studies have included ablations performed with conventional and 3D mapping, data on procedures performed in the 3D mapping era are limited.

We aimed to investigate the effect of aortic valve function and integrity of RFA of coronary cusp PVCs.

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METHODS

Ethics

The study protocol was approved by the Bursa High Specialization Training and Research Hospital Clinical Researches Ethics Committee (Date: 03.2020, Decision No: 2011-KAEK-25 2020/03-21). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population

A total of 54 consecutive patients who underwent catheter ablation for PVCs were enrolled in this study at Bursa High Specialization Training and Research Hospital. Inclusion criteria were as follows: 1) patients with frequent PVCs as indicated by a total PVC count of >10000 beats during 24-h Holter electrocardiography monitoring, 2) patients having LV ejection fraction (LVEF) <50%, 3) patients who were resistant to antiarrhythmic drugs, beta blockers, or nondihydropyridine calcium channel blockers (for at least 6 months), 4) patients aged >18 years. The ablation procedure was considered to be successful when there was >80% decline in PVCs with the same morphology during 24-h electrocardiogram (ECG) holter monitorization at the 3-month follow-up. Exclusion criteria of this study were follows: 1) ischemic cardiomyopathy, severe valvular heart disease, LV hypertrophy and other cardiomyopathies 2) people referred to anti-arrhythmic drug treatment. Demographic, clinical, and laboratory characteristics of the study patients were recorded from patient files. Electrocardiography or 24-h ECG Holter recording electrocardiography data of the entire study population were also obtained. Details of the study were explained to patients and written informed consent was obtained before participation.

Echocardiography

Two-dimensional transthoracic echocardiography (Philips i33, Eindhoven, The Netherlands) was performed before and three months after the ablation procedure in accordance with the guidelines of the American Society of Echocardiography 6. A standard examination protocol was followed by a detailed assessment of the LV diastolic and systolic functions and left atrium (LA) functions. LVEF was determined by the biplane Simpson method. LV diastolic functions (LVDD) were assessed by pulsed-wave Doppler analysis of the diastolic mitral inflow and Tissue Doppler imaging of the LV wall at the basal segments of the lateral and septal walls. Conventional Doppler parameters along with LVDD grading were assessed, calculated, and recorded. Structure of the aortic valve, coaptation features, presence of AR and degree of regurgitation (classified as non-AR, mild-AR, moderate-AR, and severe-AR) were evaluated by echocardiography. One or more degree increase in the AR was accepted significant. These patients with significant increase in AR were evaluated by trans-esophageal echocardiography (TEE) after the patients' informed consent was taken.

Electrophysiological Study and Radiofrequency Catheter Ablation Procedure

All antiarrhythmic drugs, except amiodarone, were discontinued for five half-lives before the procedure. Endocardial signal and surface electrocardiography data were recorded using the EP Tracer device (Medtronic, Inc., USA). A 3D electro-anatomic map was plotted using the CARTO 3 D Mapping System (Biosense-Webster, CA, USA), NAVX (St Jude Medical, MN, USA) or by noncontact mapping (Ensite Array, St Jude Medical). All mapping was performed after heparin bolus, maintaining an activated clotting time ≥200 s. The aortic cusp sites were mapped via a retrograde aortic approach. If no PVCs were detected or in case of only rare PVCs, intravenous isoproterenol (1–3 μg/min) was administered to facilitate the detection of PVCs. Ablation was performed using an irrigated-tip catheter contact sense catheter (Thermo-cool-Smart Touch, Biosense-Webster, Inc., CA, USA), an open-irrigated noncontact sense catheter (3.5-mm tip Thermocool or Thermocool SF, Biosense-Webster), and a FlexAbility catheter (Endosense / Abbott, St. Paul, Minnesota, USA). The target site for the ablation was determined by the earliest bipolar electrogram preceding the QRS onset, the initial QS morphology for unipolar electrogram during PVCs and/or the excellent pace map (>11/ 12 leads). When the earliest ventricular activation site was recorded at the aortic cusp, selective angiography of the coronary artery and aorta was performed to assess the anatomical relationships between these structures and the location of the ablation catheter. Acute ablation success was defined as the absence of the clinical PVC at 30 min after the last RFA delivery.

Follow-Up

After three months following the ablation of PVCs two-dimensional transthoracic echocardiography was performed. One or more degree increase in the AR was accepted significant. These patients with significant increase in AR were evaluated by TEE.

Statistical Analysis

All statistical analyses were performed using the SPSS 23.0 software package for Windows, version 23.0 (IBM Corp., Armonk, New York, United States). Whether the distribution of continuous variables was normal or not was evaluated with the Kolmogorov–Smirnov test. Continuous variables were expressed as mean±SD or median (interquartile range). Categorical variables were expressed as numbers and percentages. Paired samples

t-test and Wilcoxon signed rank test were used to compare the variables in pre-ablation and post-ablation period. Relationship among post-ablation AR status and LVEF value, procedure time, total RFA duration and maximum RFA output were determined using correlation analysis and Spearman correlation coefficient was reported. P-value <0.05 was considered significant.

RESULTS

Fifty-four consecutive patients were enrolled in the study. The mean age of the patients was 44.6±12.0 years and the male gender ratio was 42.6%. The detailed demographic, clinical and laboratory characteristics of the study population are summarized in Table 1. PVCs originate from right coronary cusp (RCC) in %12.9 of patients, left coronary cusp (LCC) in %59.3 of patients, RCC-LCC commissure in % 27.8 of patients. Total procedure time was 136.9±33.2 minutes and RFA time was 14.9±11.4 minutes.

Changes in echocardiographic parameters after RFA were summarized in Table 2. Statistically significant increases were observed in the LVEF, mitral A wave after RFA. There is not a remarkable change in post-ablation AR degree when compared to pre-ablation values (p<0.05). In a patient with moderate AR before ablation, no worsening was observed three months after RFA and this was confirmed by TEE. Post-procedural complication rate was 1.9% with vascular access site hematoma at one patient.

DISCUSSION

This study revealed that there is not any increase at AR degree and presence after RFA of cusp PVCs.

RFA itself, through electrical heating, causes myocardial damage. Histologically, this damage results in coagulation necrosis of the myocardium, basophilic staining with evidence of intracellular calcium overload, contraction bands in the sarcomeres and nuclear pyknosis.[7] In the eighth week after ablation, the necrotic area is replaced by fibrotic tissue, adipose tissue, and cartilage tissue and may be enveloped by chronic inflammation.[8]

Table 1. Basal characteristics of study population

Variables	All population n=54
Age, years	44.6±12.0
Male gender n (%)	23 (42.6)
Body mass index, kg/m²	24.6±2.9
Risk factors, n (%)	
Diabetes mellitus	7 (12.9)
Hypertension	10 (18.5)
Hyperlipidemia	11 (20.4)
Smoking	16 (29.6)
Prior history of ablation, n (%)	5 (9.3)
ECG findings	
Heart rate, beats/min	69.0±18.0
Intrinsicoid deflection time, ms	71.5±11.6
Max deflection index, %	0.5±0.1
Maxium QRS duration, ms	136.5±9.2
Pseudo-delta, n (%)	7 (13.0)
Ventricular premature complex burden in 24-h Holter monitor, %	21,5 (9.0-33.0)
Cardiovascular drugs, n (%)	
Calcium channel blocker use	17 (31.5)
Beta blocker use	23 (42.60)
Amiodarone use	10 (18.5)
Propafenone use	21 (38.9)
Any antiarrhythmic	45 (83.3)
Anti-arrhythmic medication per patient	1.4±0.7
TSH levels, mIU/L	1.4 (0.5-3.9)
Potassium levels, mEq/L	4.5 (3.4-5.5)
Calcium leves, mg/dL	9.8 (9.0-10.4)
Catheter ablation techniques, n (%)	
Carto	36 (72.2)
Ensite presicion/Nav X	18 (27.8)
Contact force sensing catheter using, n (%)	
Yes	10 (18.5)
No	44 (81.5)
Ablation site, n (%)	
Right coronary cusp	7 (12.9)
Left coronary cusp	32 (59.3)
Right / left coronary cusp	15 (27.9)
Non coronary cusp	0
Procedural parameters	
Ablation success, n (%)	45 (83.3)
Radiofrequency time, min	14.9±11.4
Total procedure time, min	136.9±33.2
Fluoroscopy time, min	16.2±10.7
Average output, W	37.0±7.7
Cardiac tamponade, n (%)	0
Cerebrovascular events, n (%)	0
Hematoma, n (%)	1 (1.9)
Coronary damage, n (%)	0

Data presented as mean±SD or median (interquartile range) or number (%). Abbreviation: ECG, electrocardiogram; TSH, thyroid-stimulating hormone.

Table 2. Changes in systolic, diastolic, and left atrial functions following radiofrequency catheter ablation (RFA)

Variables	Pre-ablation	Post-ablation	p
Left ventricular ejection fraction, %	47.9±5.6	53,4±4,3	<0.001
Left atrium end-systolic antero- posterior diameter, mm	33.4±3.7	31.3±3.7	0.009
Mitral E velocity, cm/sec	81 (63-142)	89 (65-130)	0.079
Mitral A velocity, cm/sec	81 (62-110)	73.50 (55-110)	0.001
E/A ratio	1.1±0.2	1.2±0.3	0.027
DT, msec	188 (165-275)	185 (146-246)	0.069
Ea average, cm/sec	85.8 (70-116)	77 (65-112)	0.083
E/Ea ratio	1.0 (0.8-1.2)	1.1 (0.8-1.3)	0.047
Aortic velocity, m/sec	1.5±0.4	1.5±0.4	0.753

Data presented as mean±SD or median (interquartile range) or number (%). Abbreviation: DT, deceleration time.

There are conflicting results in the literature about the effect of RFA on aortic valve functions and integrity. Mainly two mechanisms are suggested for iatrogenic AR development. One explanation is that; mechanical compression and stretching of the aortic leaflets by the catheter tip and shaft. Catheter inserted into the LV through either the center of the aortic cusps or the non-coronary cusp-RCC commissure with the catheter bent in a "U" shape. This mechanism includes distortion of coaptation area of the aortic valve and results in especially central AR formation. The second explanation is that the RF energy given during ablation disrupts the valve functions based on the changes at the cellular level mentioned above.[9]

In a previous study by Edward et al.[4] assessing the effect of RFA on valves for VES of papillary muscle and valve origin, the presence of AR was evaluated in 84 cases of VES of aortic valve origin. An increase of two or more degrees of AR was considered significant. As a result, no significant change was found in AR levels before ablation and at least 6 months after ablation.[4] In the prospective multi-center AVATAR (Aortic Cusp Ventricular Arrhythmias: Long Term Safety and Outcome from a Multi-center Prospective Ablation Registry) study, 103 patients who underwent ablation of the aortic cusp region for ventricular arrhythmias were evaluated. In the study, "zero fluoroscopy" (using electro-anatomical mapping (EAM) and not using fluoroscopy), "EAM with fluoroscopy" and "conventional fluoroscopy" methods were applied. Aortic valve complications were divided into major (leaflet perforation, significant AR or stenosis) and minor (mild / moderate AR, stenosis, other valve abnormalities). Major complications were never seen, while 16% of patients had clinically non-significant aortic valve degeneration (usually valve margin thickening or fibrosis, less frequently mild AR). Mild/moderate aortic valve thickening and mild AR were not associated with the target ablation site and ablation details. In summary, it is concluded that ablation of the aortic valve area is safe.[10] Hoffmayer et al.[11] did not find any worsening of AR or aortic root complications in a group of patients who underwent ablation of the aortic cusp region under intracardiac echocardiography guidance for ventricular arrhythmia. In our study, similar to the findings of Edward et al.4 and Hoffmayer et al.[11] no clinically significant increase in AR related to the aortic valve was observed after ablation and at 3-month follow-up. In 1 patient, no increase in moderate AR was observed, confirmed by TEE. Minor complications reported in the AVATAR study were not found in our study.

Kis et al.[5] reported a case that aortic valve leaflet rupture following RFA of LV originated PVCs at a 72 years old man. This complication has been attributed to the mechanical effect of the catheter rather than the effect of RFA. In a study by Shinoda et al.[12] involving 32 patients who underwent ablation for idiopathic ventricular arrhythmia originating from the aortic cusp region and evaluating the presence of AR before and after the procedure, mild AR was observed in 6 patients, and there was no significant increase in the degree of AR in those who developed AR at a mean follow-up of 16.0±3.6 months. In addition, no AR was observed in patients who underwent RFA only above the valves.AR presence was found to be related to duration of the procedure and delivered energy amount during RF, with the highest risk with longer duration and highest power RF energy. In conclusion, the development of AR was found to be associated with concomitant and diffuse ablation above and below the valve, and also with mechanical damage due to catheter manipulation. In addition, AR was found to occur from the aortic valve center or the LCC-NCC junction.[12] In our study, we did not observe any degree of regurgitation of the aortic valve or any abnormality in the valve structure due to ablation or any other cause. The mean RFA time was 24.4±14.1 minutes in this study, whereas it was 14.9±11.4 minutes in our study. According to the data obtained from the study, since the development of AR was found to be associated with longer RFA duration, the shorter duration of RFA in our study may be related with the absence of AR development. Our study demonstrated that aortic cusp PVC ablation is a safe procedure with a very low incidence of complications and does not increase AR.

Study Limitations

Some limitations should be taken into cognizance before interpreting the results of the study. Firstly, our study is a single-center study and the number of patients is relatively small. Secondly, intracardiac echocardiography, which is used in some centers, was not used during our RFA procedures. Intra-procedural cardiac imaging may yield different results in the acute phase and procedure planning can be made accordingly. Third, in longer follow-up, it is not clear whether valvular pathology will develop and long-term follow-up results are required. Finally, transthoracic echocardiography or cardiac magnetic resonance imaging may detect newly developing valvular pathologies that are not visible on transthoracic echocardiography. Therefore, the use of these imaging modalities may be considered in selected patients.

CONCLUSION

In our study, no significant AR development was observed in aortic cusp-induced VES ablation. Thus, ablation of PVC originating from the aortic cusp region appears to be a safe procedure with a very low incidence of complications and does not increase AR.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Bursa High Specialization Training and Research Hospital Clinical Research Ethics Committee (Date: 03.2020, No: 2011-KAEK-25 2020/03-21).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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